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# Decomposing the Forces Between Bilayers using All-atom Simulations

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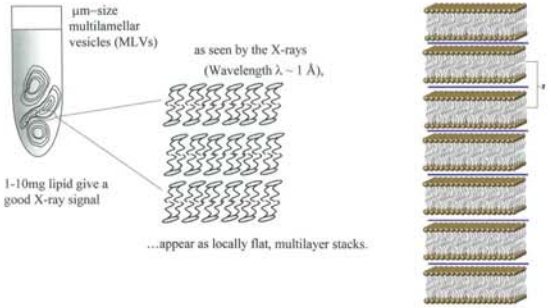
## Introduction

### Multilayer Stacks Studied Experimentally




### Continuum Theory of Multilayer Stack Interactions

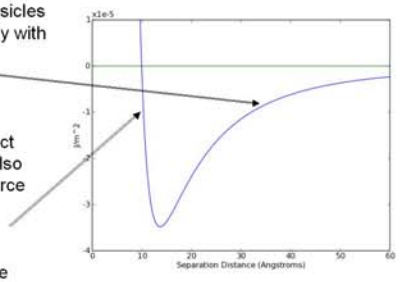
Long-range van der Waals attraction because vesicles do no swell indefinitely with added solvent

but…

Bilayers remain distinct with little solvent so also hydration repulsive force

and…

Confinement repulsive forces due to damping of undulations

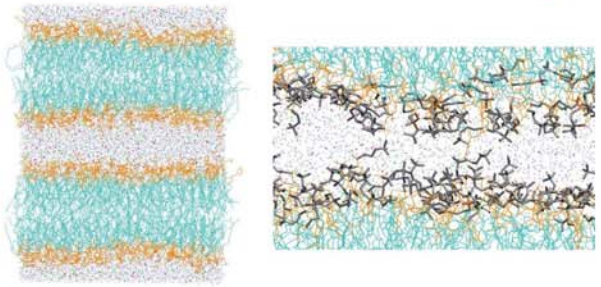



Adapted from Marcelja et al., Langmuir 2000

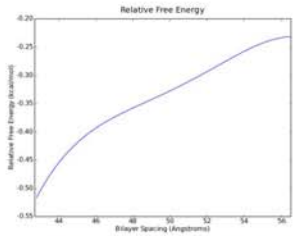
## Simulation Setup and Methods

- Double bilayer system per simulation cell to maintain membrane potential (independent water baths)
- 256 POPC lipids per bilayer
- Equal number of salts per bath
- Bilayer to bilayer distance constrained with a harmonic potential (spring constant of 2 kcal/(mol*angs$^2$))
- Constant surface area of 64 Ang$^2$/lip
- Run NVT so as not to impose pressure restraints in the z direction
- Full PME electrostatics
- Potential of mean force generated using Weighted Histogram Analysis (WHAM)
- Run in LAMMPS using CHARMM potential
- 10 ns of simulation/day possible on Sandia supercomputer

## Calculating Free and Interaction Energies



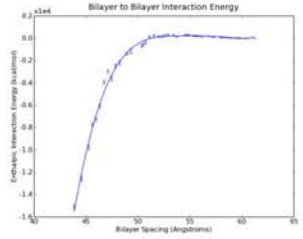
### Bilayers Attract as They Approach Each Other (Preliminary Result)




200+ windows run to ensure good sampling and overlap

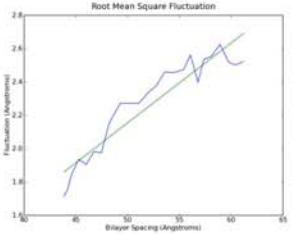
Results fit to a 4th order polynomial

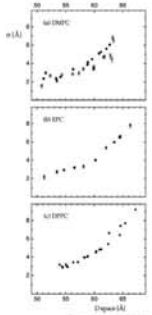
### Bilayers Interact More Strongly as They Get Closer Together




Large energies indicate that other compensating energy terms are involved in the final free energy

### RMS Fluctuation in Bilayer Separation Agree with Experiment

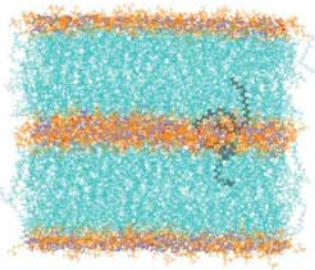


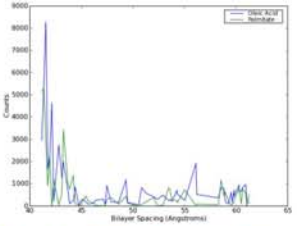
Petrache et al., Phys Rev E, 1998

## Microscopic Behavior

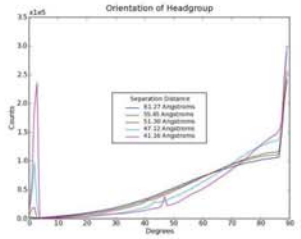
### Lipid Tails Move into the Headgroup Region as Bilayers Move Closer



### The Number of Lipid Splay-like Events Increases as Bilayers Near Contact




### Bimodal P-N Dipole Distributions Develop as Bilayers Approach Each Other




## Conclusions

- Bilayers in our simulation setting feel an attractive potential as they move closer together. This pattern is echoed in the bilayer-to-bilayer interaction energy.
- RMS fluctuation values of bilayer separation agree well with experimental values.
- There is a strong increase in splay-like events when the bilayers are quite close together.
- The P-N dipole of the lipid headgroups orients more strongly near 90 degrees and 0 degrees when the bilayers are closer together. The cluster at the 0 degree end is not seen in the analogous coarse-grain simulations.